

CLAIMS

1. Method for the humanization of the VH and VL variable regions of an animal antibody of known sequence, comprising the steps of:

5 a) if not available, obtaining the crystallographic structure of the VH and VL regions of the animal antibody;

b) pre-selecting a series of 0 to n possible frameworks acceptors of human origin or humanized antibodies, whose structure was determined experimentally with a resolution of no less than 3 Å, based on the highest level of homology and identity with the primary sequence of the framework of the animal antibody;

10 c) conducting a structural comparison between the VH and VL variable regions of the animal antibody and the regions VH and VL obtained in b), respectively and calculating for each comparison the RMS, to identify the region VH and the region VL of human origin with the smaller RMS;

15 d) inserting in appropriate position the sequences of the regions CDR of the animal antibody in the human sequences identified in c);

e) if necessary, retromutate one or more amino acid residues of the human VH and VL regions identified in c).

2. Method as claimed in claim 1 wherein the modifications of the antibody take place with recombining DNA techniques.

20 3. Method as claimed in claim 1, wherein the animal antibody is an anti-NGF antibody.

4. Method as claimed in claim 2, wherein the anti-NGF antibody, preferably it is the alpha D11 antibody, and the humanized sequences essentially have the following sequences: VH: Hum alpha D11 VH (SEQ ID No. 17) and VL: Hum alpha D11Vk (SEQ ID No. 18).

25 5. Method as claimed in claim 1, wherein the animal antibody is an anti-TrkA antibody.

6. Method as claimed in claim 4, wherein the anti-TrkA antibody is the MNAC13 antibody, and the humanized sequences essentially have the following sequences: VH: HumMNAC13VH (SEQ ID No. 37), and VL: Hum MNAC13Vk (SEQ ID No. 38).

30 7. Humanized animal antibody obtainable according to the method as claimed in any one of the previous claims.

8. Anti-NGF humanized animal antibody obtainable according to the method as claimed in any one of the previous claims.

9. Anti-TrkA humanized animal antibody obtainable according to the method as claimed in claims 5 or 6.